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PATENT

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05/3/05
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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

Applicant: Granger, et al.
Serial No.: 10/007,869
Filed: November 8, 2001
For: STABLE SKIN CARE PRODUCT CONTAINING A RETINOID AND A
RETINOID BOOSTER SYSTEM IN A DUAL COMPARTMENT PACKAGE

Group: 1617
Examiner: Jiang, Shaojia A.

MAY 3, 2005

BRIEF FOR APPELLANTS

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I. REAL PARTY IN INTEREST

The Real Party in Interest in this Appeal is Unilever Home & Personal Care USA, Division of Conopco, Inc., a corporation of the State of New York.

II. RELATED APPEALS AND INTERFERENCES

Neither the Appellants, their legal representatives nor the Assignee are aware of any other Appeals or Interferences relating to the present Appeal.

III. STATUS OF CLAIMS

This Appeal is taken from the Final Rejection of claims 1, 2, 4 through 7, 9 through 12, and 14 through 18, the pending claims in the application. Claims 3, 8 and 13 had been canceled. A copy of the appealed claims is attached to this Brief as an Appendix.

IV. STATUS OF AMENDMENTS AFTER FINAL

An Amendment after the Final Rejection was filed on January 26, 2005. The Amendment presented arguments for patentability and no claims were amended after Final.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The invention set forth in independent claim 1 on appeal is directed to a stable skin care product comprising:

a first composition comprising about 0.001% to about 10% of a retinoid selected from the group consisting of retinyl esters, retinol, retinal, and mixtures thereof;

a second composition comprising about 0.0001% to about 50% of at least one retinoid booster selected from the group consisting of CITRAL, CITRONELLOL, COCAMIDE DEA, DAMASCONE, GERANIOL, 18b GLYCERHETINIC ACID, 8 OH QUINOLINE, N LAURY SARCOSINE, LINALOOL, ALPHA IONONE and LINSEED OIL;

a first compartment for storing the first composition, wherein the first compartment keeps the first composition out of contact with oxygen;

wherein the first compartment is made out of aluminum; and

a second compartment for storing the second composition, the first and second compartments being joined together;

thereby avoiding chemical degradation of said first composition that would be caused by contact with said second composition.

The claimed invention as set forth in independent claim 6 is directed to a stable skin care product, similar to that of claim 1, with a more specific range of retinoid at about 0.01 % to about 1 % and specifying that the booster boosts a benefit provided by retinoid.

The claimed invention as set forth in independent claim 11 is directed to a stable skin care product, similar to that of claim 6, with a more specific range of retinoid at about 0.001 % to about 10 % and also specifying that the first and second compartments are made out of aluminum.

The independent claims herein are further limited by dependent claims, some of which are directed to: i.e., Claim 18, the booster alpha-ionone from the Table on page 37 of the Specification; i.e., 2, 7 and 12, retinoid combinations with *at least 2 boosters*. Claim 16 is directed to a combination of at least two boosters where one is climbazole and another is selected among alpha-ionone, damascenone and mixtures.

Claims 5, 10, and 15 are directed to a method of mimicking the effects of retinoic acid using the products of the independent claims. An unexpected result of the present invention is that compositions that do not contain retinoic acid behave analogously to treatment with retinoic acid (i.e. mimick), as if they did contain the most active form of retinoid, i.e., retinoic acid, while maintaining retinoid stability over time.

According to a further aspect of the invention, Claims 4, 9, and 14, there is provided are directed to a method for conditioning skin by applying topically to the skin the product as described in claims 1, 6 and 11, respectively.

Claim 17 specifies the emollient.

An unexpected result as shown in the Specification and Declaration is that the specified retinoid boosters, despite boosting the effect of specified retinoids on the skin, tend to *destabilize* the specified retinoids in the composition. The claimed retinoid boosters are among a specific list that has been demonstrated *with objective evidence on p 37 of the Specification* and in the Rule 132 Declaration to de-stabilize retinoids to a greater extent than the retinoids would be unstable in the absence of the boosters, i.e., there is a greater stability problem. The 2d column of the Table on p 37 lists the fold increase in rate of retinol loss compared to retinol without booster. The retinoid/retinoid booster combinations, *both of which are intended for the same skin benefit and to be applied substantially at the same time*, are maintained in separate compartments of a dual-compartment package and the retinoid composition is kept out of contact with oxygen to promote its stability against chemical degradation and to avoid further instability that would be caused by contact with retinoid boosters.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The issues raised in this appeal is primarily one of fact and of the type normally encountered in connection with a rejection made under 35 USC §103. In particular, the issues are as follows:

Would one of ordinary skill in the art, upon reading Burger et al., U.S. Patent No. 5,759,556 and Granger et al., U.S. Patent No. 5,716,627 find it obvious to employ the unique combination of:

a first composition comprising about 0.001% to about 10% of a retinoid selected from the group consisting of retinyl esters, retinol, retinal, and mixtures thereof;

a second composition comprising about 0.0001% to about 50% of at least one retinoid booster selected from the group consisting of CITRAL, CITRONELLOL, COCAMIDE DEA, DAMASCONE, GERANIOL, 18b GLYCERHETINIC ACID, 8 OH QUINOLINE, N LAURY SARCOSINE, LINALOOL, ALPHA IONONE and LINSEED OIL;

a first compartment for storing the first composition, wherein the first compartment keeps the first composition out of contact with oxygen;

wherein the first compartment is made out of aluminum; and

a second compartment for storing the second composition, the first and second compartments being joined together;

thereby avoiding chemical degradation of said first composition that would be caused by contact with said second composition, as set forth in the claimed invention, to produce a superior stable skin care product?

A similar issue is raised with respect to the claimed invention as set forth in independent claim 6, directed to a stable skin care product, similar to that of claim 1, with a more specific range of retinoid at about 0.01 % to about 1 % and specifying that the booster boosts a benefit provided by retinoid.

A similar issue is raised with respect to the claimed invention as set forth in independent claim 11 is directed to a stable skin care product, similar to that of claim 6, with a more specific range of retinoid at about 0.001 % to about 10 % and also specifying that the first and second compartments are made out of aluminum.

VII. ARGUMENT

The Examiner has rejected claims 1-2, 4-7, 9-12, and 14-18 under 35 USC §103 as being unpatentable over Burger et al. (USPN 5,759,556) and Granger 5,716,627 in view of Liu et al. (USPN 5,976,555) and Soares et al. (USPN 5,914,116) and further in view of Remington's Pharmaceutical Sciences (Remington).

In the rejection, the Examiner maintains, in summary, that Burger '556 disclose a skin conditioning composition comprising retinol or retinyl ester in combination with alpha-ionone and damascone; and a method of conditioning skin; and a composition further comprising emollients; and that the compositions would be stored in a suitable container. The Examiner further mentions that the Granger '627 reference describes compositions that comprise retinoids, azoles, and fatty acid amides stored in a suitable container. Moreover, the Examiner again continues by mentioning that the use of a first compartment for storing retinoid kept out of contact with oxygen and the second compartment for storing boosters (e.g., *alpha-ionone*), and the first and second compartments being joined together; and avoiding chemical degradation of retinol or retinyl ester in the first composition that would be caused by contact with boosters (e.g., *alpha-ionone*) in the second composition are not described in the Burger '556 and Granger '627 references, but believes that the deficiencies of the Burger and Granger references are cured by the Liu et al. reference which discloses that retinoids are

oxidatively unstable; by Suares et al., U.S. Patent No. 5,914,116 which discloses a first and second composition stored in separate containers joined together; and by the Remington reference which discloses the use of aluminum containers in pharmaceutical products. In this regard, the Examiner maintains that the 35 USC §103 rejection is proper and should be made final.

Notwithstanding the Examiner's apparent position to the contrary, it is, again, the Applicants' position that the presently claimed invention is patentably distinguishable from the above-described for at least the following reasons.

The present invention, again, as set forth in independent claim 1, is directed to a a stable skin care product comprising:

a first composition comprising about 0.001% to about 10% of a retinoid selected from the group consisting of retinyl esters, retinol, retinal, and mixtures thereof;

a second composition comprising about 0.0001% to about 50% of at least one retinoid booster selected from the group consisting of CITRAL, CITRONELLOL, COCAMIDE DEA, DAMASCONE, GERANIOL, 18b GLYCERHETINIC ACID, 8 OH QUINOLINE, N LAURY SARCOSINE, LINALOOL, ALPHA IONONE and LINSEED OIL;

a first compartment for storing the first composition, wherein the first compartment keeps the first composition out of contact with oxygen;
wherein the first compartment is made out of aluminum; and

a second compartment for storing the second composition, the first and second compartments being joined together;

thereby avoiding chemical degradation of said first composition that would be caused by contact with said second composition.

Independent claim 6 is directed to a stable skin care product, similar to that of claim 1, with a more specific range of retinoid at about 0.01 % to about 1 % and specifying that the booster boosts a benefit provided by retinoid.

Independent claim 11 is directed to a stable skin care product, similar to that of claim 6, with a more specific range of retinoid at about 0.001 % to about 10 % and also specifying that the first and second compartments are made out of aluminum.

The independent claims herein are further limited by dependent claims, some of which are directed to: i.e., Claim 18, specifically the booster alpha-ionone from the Table on page 37 of the Specification; i.e., 2, 7 and 12, retinoid combinations with *at least 2 boosters*. Claim 16 is directed to a combination of at least two boosters where one is climabazole and another is selected among alpha-ionone, damascenone and mixtures.

Claims 5, 10, and 15 are directed to a method of mimicking the effects of retinoic acid using the products of the independent claims. An unexpected result of the present invention is that compositions that do not contain retinoic acid behave analogously to treatment with retinoic acid (i.e. mimick), as if they did contain the most active form of retinoid, i.e., retinoic acid, while maintaining retinoid stability over time.

According to a further aspect of the invention, Claims 4, 9, and 14, there is provided a method for conditioning skin by applying topically to the skin the product as described in claims 1, 6 and 11, respectively.

In contrast and as already made of record, the Burger et al. reference, the primary reference, does not even suggest the need for stable cosmetic compositions that attenuate the existing problems of retinoid stability in the presence of boosters. There is no teaching whatsoever in the Burger reference to employ anti-oxidants as described in the present invention.

The Examiner correctly admits that the Burger and the Granger '627 references do not describe the use of a first compartment for storing retinoid kept out of contact with oxygen, and a second compartment for storing boosters (e.g., alpha-ionone), and the first and second compartments being joined together; and avoiding chemical degradation of retinoid in the first composition that would be caused by contact with boosters in the second composition. In view of this, the Examiner relies on the Liu et al. and Soares et al. references, and further in view of Remington's. Again, there is no teaching whatsoever in the secondary references that even remotely suggests the need or solution for stabilizing retinoid compositions in the presence of retinoid enhancing actives as described in the present invention. Moreover, there is no teaching

whatsoever in the combination of references relied on by the Examiner that even remotely suggests that boosters destabilize retinoids to a greater degree than retinoids alone would be unstable, and therefore none of the references teach or suggest a solution, in particular, a dual compartment container made of aluminum as set forth in the claims.

Liu et al. *at most* merely restate the problem *and fail to address the further instability contributed to retinoids by the presence of boosters*. Liu et al. *at most* merely state an invitation to invent by restating that retinoids are unstable. Liu et al. do not address the problem to which the present invention is addressed, i.e., alleviating the additional instability contributed by boosters. (At most, Liu et al. provide a different solution – i.e. formulating in an emulsion with a specifically defined chemical stabilizer system, but all in one composition.) The combination cited references does not arrive at the subject matter of the present invention as claimed. Although Liu et al. describe a container for storing the composition so that it is out of contact with oxygen, the container is described in combination with a retinoid composition with an emulsifier system and a co-emulsifier alone and does not protect the retinoid from degradation due to contact with retinoid boosters.

Further according to the Examiner, Soares et al. (USPN 5,914,116) teaches a first and second composition stored in separate containers joined together. However,

the product of Soares et al. includes a first composition for obtaining a first skin benefit (e.g., Vitamin A palmitate) and a second composition for obtaining a second and different benefit, "the first and second actives and benefits being different from one another;" and the two compositions are part of a regimen teaching their application at different times of day. See Col. 2, lines 1-5. The Examiner admits that Soares et al. (USPN 5,914,116) does not teach that the first and/or second compartments keep the respective compositions out of contact with oxygen. Neither do Soares et al. teach that the two compartments are made of aluminum, nor that the two compositions aimed at the same skin benefit and intended to be applied at substantially the same time.

As discussed above, Burger et al and Granger et al. are insufficient primary references and the secondary references do not remedy its deficiencies. Furthermore, there is no motivation to combine Burger and Granger with Remington, Soares et al. and Liu et al. Remington at p. 1511 admits, "The choice of containers and closures can have a profound effect on the stability of many pharmaceuticals."

Accordingly, it would not have been obvious to a person of ordinary skill in the art at the time the invention was made to employ two compartments for separately storing retinol or retinyl ester in a first composition and booster in the second composition in order to stabilize retinoids against the instabilities caused by the presence of boosters.

**IN PARTICULAR, CLAIM 16 IS NOT OBVIOUS OVER THE
MULTIPLE COMBINED REFERENCES**

Claim 16 specifies a booster combination of **climbazole** (B5) with **alpha-ionone** (B1) and/or **damascenone**.

Burger '556 do not disclose *climbazole* and Granger '627 is cited for disclosing a skin conditioning composition comprising a) retinol or retinyl ester, b) azole, e.g., *climbazole*, c) a fatty acid amide such as linoleoyl-DEA. However, admittedly, Granger et al '627 does not disclose the first compartment for storing retinol or retinyl ester kept out of contact with oxygen, and the second compartment for storing azole (e.g. *climbazole*), and the first and second compartments being joined together; and avoiding chemical degradation of retinol or retinyl ester in the first composition that would be caused by contact with boosters (e.g. *climbazole* or *alpha ionone*) in the second composition.

As stated previously, the independent claim 11 and claim 16 dependent thereon relate to specific booster compounds that are shown to de-stabilize the claimed retinoids to a greater extent than the degree of instability in the absence of the boosters. See the table on page 37 of the Specification. For example, the results in the Table show that *alpha-ionone* increases the rate of retinol loss by a factor of 1.3. According to the accompanying Declaration, retinol is only 2/3 as stable in the presence of citral. Similarly, it can be seen that all the claimed boosters significantly increase the rate of retinol loss. Therefore, the presence of the boosters necessitates separate compartments for the two compositions, more so than the cited art. These are unexpected results.

Evidence of Unexpected Results Has Been Presented

To demonstrate unexpected results, attention is drawn to the Table on page 37 of the specification as originally filed, as well as the Rule 132 Declaration of Dr. lobst. The results of the table demonstrate that *alpha-ionone* (B1 booster) increases the rate of retinol loss by a factor of 1.3 according to compositions of the present invention.

The data show that all the claimed boosters significantly increase the rate of retinol loss. According to the accompanying Declaration, retinol is only 2/3 as stable in the presence of citral. Dr. lobst states that, based on analysis of the data presented, it is clear that Retinol stability is significantly diminished in the presence of boosters, creating a greater necessity for its stabilization than in the absence of boosters.

Therefore, the presence of the boosters necessitates separate compartments for the two compositions, more so than the cited art. Neither Liu '555 nor Soares, nor any of the many cited references alone or in any combination, even in the slightest way suggest that boosters further destabilize retinoids. In other words, neither Liu '555 nor Soares, nor any of the many cited references alone or in any combination, suggest a way to protect the retinoid from degradation due to contact with retinoid boosters. The claimed invention is clearly not obvious in view of the cited art, and for the reasons above, the 103(a) rejections should be reconsidered and withdrawn. Additionally, Applicants have shown the advantages of employing more than a single booster with

respect to increase in CRABP II production. This advantage is supported by Dr. Iobst's Declaration while demonstrating the instability due to the presence of boosters.

In view of the above, it is again clear that the Examiner has not established a *prima facie* case of obviousness as required under 35 USC §103. When establishing a *prima facie* case of obviousness, it is fundamentally improper to gloss over important and critical claim limitations. The "invention as a whole" must be considered, including all limitations of the claimed invention. *In re Boe*, 184 U.S.P.Q. 38, 40 (C.C.P.A. 1974) ("..., all limitations must be considered and that it is error to ignore specific limitations distinguishing over the references").

It is improper to pick and choose pieces of a variety of art to come up with a rejection as in the Office Action. There must be some suggestion or motivation for combinations of the references, so as to come up with the claimed invention, which must be viewed as a whole.

Burger fails to disclose climbazole. Burger and Granger fail to disclose the first compartment for storing retinol or retinyl ester kept out of contact with oxygen; and first and second compartments being joined together; and avoiding chemical degradation of retinol or retinyl ester in the first composition. Nor do Burger, Liu and Soares disclose

the first compartment made of aluminum. Remington's is cited for storage of pharmaceuticals to address the aluminum container limitation.

The Office Action position notwithstanding, Applicants respectfully submit that the significant diminution in retinoid stability in the presence of boosters was not known and is unexpected over Liu et al. and Soares et al. alone or in any combination with each other or the other cited references. Liu et al. and Soares et al. have nothing to do with boosters. On the other hand, the present invention teaches the need for stabilizing retinoids in the presence of boosters and evidence in the Examples of the Specification and in the Declaration provides objective support for the unobviousness of the present invention.

If fact, none of the references cited in the Office Action teaches or suggests the need or the solution for stabilizing retinoid compositions in the presence of retinoid enhancing actives. Therefore, although dual purpose single formulation cosmetic products have been developed in the cited art, only in hindsight, with the benefit of the disclosure of the present invention, is the need for stable cosmetic compositions that attenuate the existing problems of retinoid stability in the presence of boosters met.

There is no suggestion in the cited art that the further destabilization of retinoids contributed by the presence of boosters was within the knowledge which was within the level of ordinary skill at the time the claimed invention was made, nor that the knowledge was generally available to one skilled in the art. Even if combined, Applicants respectfully submit that, since the independent claims are in condition for allowance, those claims that depend from them are also in condition for allowance.

An obviousness rejection is proper only when "the subject matter as a whole would have been obvious at the time the invention was made ..." (emphasis added). 35 U.S.C. 103. Applicants respectfully submit that the Office Action has improperly chosen certain aspects of one reference and combined them with aspects of other references, without showing where the motivation is to combine them to come up with the subject matter of the present invention as a whole, within the meaning of 35 U.S.C. 103. Applicants submit that the pending claims are not obvious over the cited references, under 35 U.S.C. 103. Reversal of this rejection is respectfully requested.

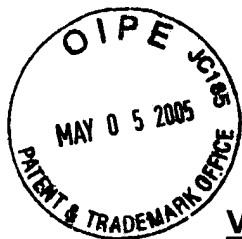
In view of the above, Appellants submit that a proper rejection under 35 U.S.C. 103 has not been made. Accordingly, reversal of the Final Rejection by the Honorable Board is appropriate and is courteously solicited.

Respectfully submitted,



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VIII. CLAIMS APPENDIX

Claim 1: A stable skin care product comprising:

a first composition comprising about 0.001% to about 10% of a retinoid selected from the group consisting of retinyl esters, retinol, retinal, and mixtures thereof;

a second composition comprising about 0.0001% to about 50% of at least one retinoid booster selected from the group consisting of CITRAL, CITRONELLOL, COCAMIDE DEA, DAMASCONE, GERANIOL, 18b GLYCERHETINIC ACID, 8 OH QUINOLINE, N LAURY SARCOSINE, LINALOOL, ALPHA IONONE and LINSEED OIL;

a first compartment for storing the first composition, wherein the first compartment keeps the first composition out of contact with oxygen;

wherein the first compartment is made out of aluminum; and

a second compartment for storing the second composition, the first and second compartments being joined together;

thereby avoiding chemical degradation of said first composition that would be caused by contact with said second composition.

Claim 2. The stable skin care product of claim 1 wherein the second composition has at least two retinoid boosters in an amount of about 0.0001% to about 50%.

Claim 3 (canceled)

Claim 4. A method of conditioning skin, the method comprising applying topically to the skin the product of claim 1.

Claim 5. A method of mimicking the effect on skin of retinoic acid, the method comprising applying to the skin the product of claim 1; wherein said effect is chosen from the group consisting of treatment of acne, wrinkles, psoriasis, age spots, discoloration, and combinations thereof.

Claim 6. A stable skin care product comprising:

a first composition comprising about 0.01% to about 1% of a retinoid to provide a first benefit; said retinoid selected from a group consisting of retinyl esters, retinol, retinal, and mixtures thereof;

a second composition comprising about 0.0001% to about 50% of at least one retinoid booster to boost the first benefit;

said retinoid booster selected from the group consisting of CITRAL, CITRONELLOL, COCAMIDE DEA, GERANIOL, 18b GLYCERHETINIC ACID, 8 OH QUINOLINE, N LAURY SARCOSINE, LINALOOL, and LINSEED OIL;

a first compartment for storing the first composition, wherein the first compartment keeps the first composition out of contact with oxygen;

wherein the first compartment is made out of aluminum; and

a second compartment for storing the second composition, the first and second compartments being joined together;

thereby avoiding chemical degradation of said first composition that would be caused by contact with said second composition.

Claim 7. The stable skin care product of claim 6 wherein the second composition has at least two retinoid boosters in an amount of about 0.0001% to about 50%.

Claim 8 (canceled)

Claim 9. A method of conditioning skin, the method comprising applying topically to the skin the product of claim 6.

Claim 10. A method of mimicking the effect on skin of retinoic acid, the method comprising applying to the skin the product of claim 6 ; wherein said effect is chosen from the group consisting of treatment of acne, wrinkles, psoriasis, age spots, discoloration, and combinations thereof.

Claim 11. A stable skin care product comprising:

a first composition comprising about 0.001% to about 10% of a retinoid to provide a first benefit; said retinoid selected from a group consisting of retinyl esters, retinol, retinal, and mixtures thereof;

a second composition comprising about 0.0001% to about 50% of at least one retinoid booster to boost the first benefit;

said retinoid booster selected from the group consisting of CITRAL, CITRONELLOL, Climbazole, COCAMIDE DEA, DAMASCONE, GERANIOL, 18b GLYCERHETINIC ACID, 8 OH QUINOLINE, N LAURY SARCOSINE, LINALOOL, ALPHA IONONE and LINSEED OIL;

a first compartment for storing the first composition, wherein the first compartment keeps the first composition out of contact with oxygen; and

a second compartment for storing the second composition, wherein the second compartment keeps the second composition out of contact with oxygen;
wherein the first and second compartments are made out of aluminum ;
and wherein the first and second compartments are joined together;

thereby avoiding chemical degradation of said first composition that would be caused by contact with said second composition.

Claim 12. The stable skin care product of claim 11 wherein the second composition has at least two retinoid boosters in an amount of about 0.0001% to about 50%.

Claim 13 (canceled)

Claim 14. A method of conditioning skin, the method comprising applying topically to the skin the product of claim 11.

Claim 15. A method of mimicking the effect on skin of retinoic acid, the method comprising applying to the skin the product of claim 11; wherein said effect is chosen from the group consisting of treatment of acne, wrinkles, psoriasis, age spots, discoloration, and combinations thereof.

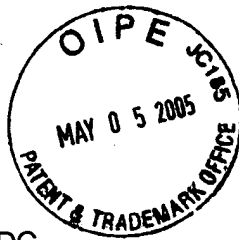
Claim 16. The stable skin care product according to claim 11,
wherein said retinoid booster is Climbazole; and
wherein said product further comprises a second retinoid booster selected from the
group consisting of alpha-ionone, damascenone, and mixtures thereof.

Claim 17. The stable skin care product of claim 1, further comprising about 0.5 % to
about 50 % of an emollient selected from the group consisting of esters, fatty acids,
alcohols, polyols, and hydrocarbons.

Claim 18. The stable skin care product of claim 1, wherein said booster is alpha-
ionone.

IX. EVIDENCE APPENDIX

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UNUS #: Y2-R554-EDG

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Granger et al.
Serial No.: 10/007,869
Filed: November 8, 2001
For: STABLE SKIN CARE PRODUCT CONTAINING A RETINOID
AND A RETINOID BOOSTER SYSTEM IN A DUAL
COMPARTMENT PACKAGE

Group: 1617
Examiner: Jiang, S. A.
Edgewater, New Jersey 07020
JULY 28, 2004

DECLARATION UNDER 37 CFR 1.132

Commissioner for Patents
Alexandria, VA 22313-1450

Sir:

I, Susanne Teklits Iobst, residing at 89 Stelling Avenue, Maywood, NJ 07607
do hereby declare that:

1. I am a citizen of the United States.
2. My educational and technical background in the field of
Biochemistry is as follows:

- (a) I received a Bachelor of Science Degree in Biochemistry from Lehigh University in 1986.
 - (b) I received a Master of Science Degree in Chemistry from Stevens Institute of Technology in 1989.
 - (c) I received a Doctorate of Philosophy from the Department of Biochemistry and Molecular Biophysics at Columbia University in 1995.
 - (d) I joined my present employer Unilever in 1986 and I currently have the title Research Scientist, located in Edgewater, NJ.
3. I have read Granger et al., US Patent Application no. 10/007,869 filed November 8, 2001.
4. The following experiments were conducted in support of the above-cited Granger et al. patent application.
5. **Retinol Stability and Clinical Assessment of CRABP II**

Clinical Methodology

Compounds were formulated in a PG/EtOH vehicle with retinol. Individual subjects were treated for two times/day for 4 days with the test compound. On the 5th day, a skin sample was taken. Protein was isolated from the skin sample and a Western blot was performed using a CRABP II antibody. The % increase in CRABP II was measured in relation to the amount of CRABP II protein that was generated from a sample containing retinol alone.

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Efficacy Data: Example A

Compound	Increase in CRABPII production
Climbazole	17%
Climbazole/Damascenone/AMEA/Cetyl Alcohol	22%

Efficacy Data: Example B

Compound	Increase in CRABPII production
2.5% cetyl alcohol	50%
0.5% quercetin	8%
2.5% cetyl alcohol, 0.2% damascenone, 0.5% quercetin	121%

Retinol Stability Data: Example 1

Compound	Retinol stability @21 days at 30 C
Retinol	62%
Retinol/Citral	40%
Retinol/citral/glycyrretinic acid/quercetin	37.6%

6. I conclude the following from these experiments:

Based on the analysis above, it is clear that Retinol stability is significantly diminished in the presence of boosters, creating a greater necessity for its stabilization than in the absence of boosters. Example 1 shows the significant decrease in retinol stability in the presence of the citral booster.

A combination of boosters gives a greater increase in CRABPII production than a single booster. With some of the combinations in the

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Tables, the size of the effect is greater than additive, indicating a strongly synergistic result.

Example A shows that combining retinol with at least two boosters, e.g., climbazole with damascenone, leads to greater increase in CRABP II production.

7. I declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code and may jeopardize the validity of the application or any patent issuing thereon.

Dated: JULY 28 , 2004

By: 
Susanne Teklits lobst

Title: Research Scientist

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to:

"Commissioner for Patents and Trademarks
Alexandria, Virginia 22313-1450"

MAY 3, 2005

Ellen Plotkin
Reg. No. 36,636
Attorney for Applicant(s)

5 / 3 /05
Date of Signature

PATENT

**IN THE UNITED STATES PATENT
AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT
APPEALS AND INTERFERENCES**

Appellant: GRANGER, et al.
Serial No.: 10/007,869
Filed: November 8, 2001
For: STABLE SKIN CARE PRODUCT CONTAINING A RETINOID AND A RETINOID
BOOSTER SYSTEM IN A DUAL COMPARTMENT PACKAGE

Group: 1617
Examiner: Shaojia A. Jiang

MAY 3, 2005

BRIEF FOR APPELLANTS

Commissioner for Patents and Trademarks
Alexandria, Virginia 22313-1450

Sir:

Enclosed herewith are three (3) copies of an Appeal Brief for Appellant.

Please charge the \$500.00 fee to our Deposit Account No. 12-1155. Any deficiency or overpayment should be charged or credited to this Deposit Account. This authorization is submitted in triplicate.

Respectfully submitted,



Ellen Plotkin
Registration No. 36,636
Attorney for Applicant(s)

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